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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/768,566	01/29/2004	Kiran K. Chada	69014-B/GJG	6434

7590 04/19/2006

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EXAMINER	
CHANDRA, GYAN	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 04/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/768,566	CHADA ET AL.	
	Examiner	Art Unit	
	Gyan Chandra	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *10-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9, 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/19/06, 1/30/06*, 2/27/06.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-9 and 17, in the reply filed on 1/30/2006 is acknowledged. The traversal is on the ground(s) that Group I, drawn to administration of sFRP-5, is also drawn to administration "of a molecule effective to stimulate expression of the sFRP-5 peptide in the subject". This is not found persuasive because the inventions are distinct from each other as explained in the previous office action mailed on 12/29/2005, and the methods of Group I and Group II have different modes of operation, and different effects. Group II requires administration of a molecule that stimulates expression of sFRP-5 peptide in a subject, whereas Group I requires administering the peptide sFRP-5 in a subject.

The requirement is still deemed proper and is therefore made FINAL.

Status of Application, Amendments, And/Or Claims

Claims 1-17 are pending.

Claims 10-16 are withdrawn from further consideration as being drawn to a nonelected Invention.

Claims 1-9, and 17 are under examination.

Priority

The instant application claims priority to US 10/630,423, filed on 7/29/2003, which claims benefit of US Provisional Application 60/398,785, filed on 7/29/2002 and US Provisional Application 60/478,206, filed on 6/12/2003. Upon reviewing these applications, the Examiner has determined that the instant application gets priority of

U.S. Provisional 60/478,206 filing date 6/12/2003, in which Applicant has first disclosed the cloning and expression of sFRP5 polypeptide.

Information Disclosure Statement

The information disclosure statements filed on 1/19/06, 1/30/06, and 2/27/2006 have been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn a method of reducing the amount of adipose tissue in a subject by administering to the subject an effective amount of an sFRP-5 peptide wherein the peptide has (i) 90 % identity to the sequence of SEQ ID NO: 1, (ii) 91 % identity to the sequence of SEQ ID NO: 1, (iii) 92 % identity to the sequence of SEQ ID NO: 1, (iv) 95 % identity to the sequence of SEQ ID NO: 1, and (v) 99 % identity to the sequence of SEQ ID NO: 1. The claims do not require that the sFRP-5 peptidesor derivative possess any particular conserved structure, or any other disclosed distinguished feature. Thus, the claims are drawn to a genus of polypeptides variant or

derivative that is defined by a large number of amino acid substitutions, deletions or insertions modifications.

To provide possession of a claimed invention, the specification must provide sufficient distinguishing identifying characteristics for the invention. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, method of making an invention or any combination thereof. The specification does not provide a definition of " a derivative" or disclose any derivative of leptin or leptin homologue. As such the genus "sFRPs with 90%, 91%, 92%, 95% and 99%" encompass any peptide, protein or agent that can reduce the amount of adipose tissue.

This is a written description rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, & 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the Awritten description inquiry, is *whatever is now claimed* (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (see Vas-Cath at page 1116).

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly & Co., 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In Regents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B (1), the court states an adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention.

As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of sFRPs peptide, variants, or homologoue and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of making a mutation. The compound itself is required. See Fiers v.Revel, 25USPQ2d 1601 at 1606 (CAFC 1993) and Amgen v.Baird, 30 Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 148 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of

written description for that broad class. Therefore, only the leptin polypeptide, but not the breadth of the claims meet the written description provision of 35 U.S.C. § 112, first paragraph.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claims 1-9 and 17are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for reducing the amount of adipose tissue in a subject by administering to the subject an effective amount of an sFRP-5 peptide of SEQ ID NO: 1 or a peptide that has (i) 90 % identity to the sequence of SEQ ID NO: 1, (ii) 91 % identity to the sequence of SEQ ID NO: 1, (iii) 92 % identity to the sequence of SEQ ID NO: 1, (iv) 95 % identity to the sequence of SEQ ID NO: 1, and (v) 99 % identity to the sequence of SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected to practice that invention.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond

that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986).

Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

The Nature of the Invention: The claims are drawn to a method for reducing the amount of adipose tissue in a subject by administering to the subject an effective amount of an sFRP-5 peptide of SEQ ID NO: 1 or a peptide that has (i) 90 % identity to the sequence of SEQ ID NO: 1, (ii) 91 % identity to the sequence of SEQ ID NO: 1, (iii) 92 % identity to the sequence of SEQ ID NO: 1, (iv) 95 % identity to the sequence of SEQ ID NO: 1, (v) 99 % identity to the sequence of SEQ ID NO: 1, and (vi) wherein the

administration is parenteral, intradermal, transdermal, transmucosal, rectal, subcutaneous, or by inhalation.

The state of the prior art and the predictability or lack thereof in the art:

Hu et al. (Bioch. Biophys. Res. Comm. 247, 287-293, 1998) teach that frizzled receptor proteins (FRPs), also known as fzrbs, are a family of secreted glycoproteins that function to modulate signaling activity of Wnt, and that they share homology with the extracellular domain of frizzled receptor. These proteins receptor play important roles in a variety of biological functions including developmental as well as pathological diseases such as tumorigenesis (page 287, right column). They suggest that one of the FRPs, FRP-2 is abundantly expressed in human and rodent adipose tissues (page 287, last paragraph). They also report that the expression of sFRP-1b in human pancreatic tissue is specific and abundant, and therefore, they predict its role in pancreatic function. Xu et al. (US 2003/0143610 A1) suggest a secreted apoptosis related protein (SARP) has some role in metabolic disorders, including, but not limited to, obesity, diabetes, insulin resistance, anorexia and catchexia (see abstract and claims 9-20). However, Umansky et al (2003/0023061 A1) disclose that SARPs play role in apoptosis related disorders [0002]. They contemplate using SARPs/ FRPs for the treatment of apoptosis related conditions comprising administering a therapeutically effective amount of pharmaceutical composition comprising SARP polypeptide (claims 37-43). Therefore, the field of FRPs is controversial, and the specification does not provide any guidance or any example showing administration of the polypeptide of SEQ ID NO: 1 or a variant thereof that can reduce the amount of adipose tissue in a human subject. Further, the

ob/ob mouse is not always a predictive model for human treatment. The leptin gene is also highly expressed in adipose tissue in mice and humans, but its role in human obesity remains controversial at present. The Ob gene product, leptin, seems to regulate food intake and energy. However, the role of leptin in body mass reduction and/or energy homeostasis is controversial and not clear. Jequier and Tappy (Physiological Rev. 79: 451-480, 1999) state that a clinical study comprising 100 subjects did not reveal any mutation in leptin gene and therefore, in most cases of obesity, does not result from a defect function of leptin in the adipose tissue (page 467, 1st paragraph of the right column). Therefore, the ob/ob mouse model is not predictive of the instantly claimed human treatment.

The amount of direction and guidance present and the presence or absence of working examples: Given the teachings of unpredictability found in the art, detailed teachings are required to be present in the disclosure in order to enable the skilled artisan to practice the invention commensurate in scope with the claims. These teachings are absent. The specification teaches that sFRP-5 is expressed in inguinal fat, epididymal fat, mesenteric fat, large intestine and brain. However, gene expression data are not conclusive and they do not suggest or confirm, that if sFRP-5 is administered, it will reduce adipose tissue in a human subject. The specification does not teach any example in a subject of reducing adipose tissue by administering the peptide. The ob/ob model or a transgenic mice (figure 7) showing gene expression in adipose tissue is not necessarily predictive of reducing adipose tissue in subjects because the role of sFRPs is still controversial. Therefore, it would require a large

amount of experimentation to determine if the sFRP-5 of SEQ ID NO: 1, or the claimed variants, would reduce the amount of adipose tissue in a subject

The breadth of the claims and the quantity of experimentation needed: Because the claims encompass a method of reducing the amount of adipose tissue in a subject by administering to the subject an effective amount of an sFRP-5 peptide, in the light of the teachings of the unpredictability found in the art discussed and because of the supra lack of sufficient teachings in applicants disclosure to overcome those teachings, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 1-9, the claim indefinite because it is unclear from the claims what sFRP-5 is because there is no structure recited

Claims 2-6 are rejected as being indefinite because claim 2 encompasses a method of stimulating expression of sFRP-5 with peptide of SEQ ID NO: 1 or variants, but the SEQ ID NO: 1 is sFRP-5.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-9 and 17 are rejected under 35 U.S.C. 102(e) as being anticipated by Xu et al. (US 2003/0143610, effective priority date 1/8/2002(60/346,523)).

The claims are drawn to a method of reducing the amount of adipose tissue in a subject by administering to the subject an effective amount of an sFRP-5 peptide wherein the peptide has (i) 90 % identity to the sequence of SEQ ID NO: 1, (ii) 91 % identity to the sequence of SEQ ID NO: 1, (iii) 92 % identity to the sequence of SEQ ID NO: 1, (iv) 95 % identity to the sequence of SEQ ID NO: 1, (v) 99 % identity to the sequence of SEQ ID NO: 1, and (vi) wherein the administration is parenteral, intradermal, transdermal, transmucosal, rectal, subcutaneous, or by inhalation.

Xu et al teach administration of a polypeptide SARP of SEQ ID NO: 2 which is 100% identical to the polypeptide of SEQ ID NO: 1 (Appendix-A) of the instant application for the treatment of metabolic disorders including obesity and diabetes comprising the SARPs polypeptides (see abstract, and claims 9-20). Xu et al do not explicitly teach reduction in an amount of adipose tissue but the administration of the

polypeptide of SEQ ID NO: 2 or a variant would inherently achieve the same effect in a subject as being instantly claimed [0176 – 0177], [0204 – 0205]. Therefore, all the limitations are met.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gyan Chandra whose telephone number is (571) 272-2922. The examiner can normally be reached on 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Eileen B. O'Hara

Gyan Chandra, Ph.D.
Art Unit 1646
11 April 2006
Fax: 571-273-2922

EILEEN B. O'HARA
PRIMARY EXAMINER

Appendix - : A

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RESULT 2
US-10-338-604-2
; Sequence 2, Application US/10338604
; Publication No. US20030143610A1
; GENERAL INFORMATION:
;  APPLICANT: Xu, Haiyan
;  TITLE OF INVENTION: METHODS FOR THE TREATMENT OF METABOLIC
;  TITLE OF INVENTION:  DISORDERS, INCLUDING OBESITY AND DIABETES
;  FILE REFERENCE: MPI01-250P1RM
;  CURRENT APPLICATION NUMBER: US/10/338,604
;  CURRENT FILING DATE:  2003-01-08
;  PRIOR APPLICATION NUMBER: 60/346,523
;  PRIOR FILING DATE: 2002-01-08
;  NUMBER OF SEQ ID NOS: 6
;  SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 2
;   LENGTH: 317
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-10-338-604-2

  Query Match             100.0%;  Score 1730;  DB 4;  Length 317;
  Best Local Similarity   100.0%;  Pred. No. 4.6e-169;
  Matches  317;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MRAAAAAGGVRTAALALLLGALHWAPARCEEYDYYGWQAEPLHGRSYSKPPQCLDIPADL 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MRAAAAAGGVRTAALALLLGALHWAPARCEEYDYYGWQAEPLHGRSYSKPPQCLDIPADL 60

Qy         61 PLCHTVGYKRMRLPNLLEHESLAEVKQQASSWLPLLAKRCHSDTQVFLCSLFAPVCLDRP 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 PLCHTVGYKRMRLPNLLEHESLAEVKQQASSWLPLLAKRCHSDTQVFLCSLFAPVCLDRP 120

Qy        121 IYPCRSLCEAVRAGCAPLMEAYGFPWPEMLHCHKFPLDNDLCIAVQPGHLPATAPPVTKI 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 IYPCRSLCEAVRAGCAPLMEAYGFPWPEMLHCHKFPLDNDLCIAVQPGHLPATAPPVTKI 180

Qy        181 CAQCEMEHSADGLMEQMCSSDFVVKMRIKEIKIENGDRKLIGAQKKKKLLKPGPLKRKDT 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 CAQCEMEHSADGLMEQMCSSDFVVKMRIKEIKIENGDRKLIGAQKKKKLLKPGPLKRKDT 240

Qy        241 KRLVLHMKNGAGCPCPQLDSLAGSFLVMGRKVDGQLLLMAVYRWDKKNKEMKFAVKFMFS 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 KRLVLHMKNGAGCPCPQLDSLAGSFLVMGRKVDGQLLLMAVYRWDKKNKEMKFAVKFMFS 300

Qy        301 YPCSLYYPFFYGAAEPH 317
              |||||||||||||||||
Db        301 YPCSLYYPFFYGAAEPH 317
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